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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,024	06/24/2003	Bradley G. Thompson	16596-001001	7648

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EXAMINER	
BROWN, TIMOTHY M	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/602,024	THOMPSON ET AL.	
	Examiner	Art Unit	
	Timothy M. Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *7,14,16-22,27 and 30-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-13,15,23-26,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/20/03; 2/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication received April 7, 2005. Claims 1-33 were restricted in the preceding action. According Applicant's election, and the response to Applicants' traverse below, claims 1-6, 8-13, 15, 23-26, 28 and 29 are under examination. Claims 7, 14, 16-22, 27 and 30-33 are withdrawn from consideration.

Priority

Applicants' claim of priority to provisional applications 60/392031 filed June 28, 2002 and 60/443188 filed January 29, 2003 is acknowledged.

Election/Restrictions

Applicants election, with traverse, of Group (I)(iv) is acknowledged. In view of the remarks below, the invention under examination is a method for detecting ras-activated neoplastic cells comprising obtaining a sample from a human, and exposing the sample to serotype 3 Dearing strain reovirus, wherein infection of the sample by reovirus indicates the presence of ras-activated neoplastic cells in the sample.

Applicants' traverse as to Groups iii and xv is persuasive. The restriction of these groups is therefore withdrawn. Applicants argue the restriction as to Groups ii and v-xv should be withdrawn because these groups are related. Applicants reason the groups are related because the specification discloses that each of the viruses can be used to detect the different forms of cancer disclosed in the specification. However, this does not demonstrate that the viruses themselves can be used together. For example, the specification does not disclose using avian reovirus (Group ii) in combination with vesicular stromatitis virus (Group xii) to detect a neoplasm. Thus, the inventions of Groups ii and v-xv are unrelated.

Applicants argue the restriction requirement as to Groups i, ii, and x-xiv should be withdrawn because examining these groups together would not create a serious burden. Applicants reason there is no serious burden because the stated groups are all drawn to oncolytic viruses. The Examiner respectfully disagrees in that an examination of the various groups would required different search terms, different cellular receptors, and different infection specificities. For the reasons stated above, the restriction requirement as to Groups i, ii, and x-xiv is maintained.

Applicants state the restriction requirement does not clearly state which claims belong to the various inventions. The Examiner regrets any confusion and addresses this lack of clarity by presenting Group I with claim numbers listed. The following groupings consider the withdrawal of the restriction of subgroups (iii) and (xv).

i. Contacting the sample with serotype 3 Dearing strain reovirus (claims 1-6, 8, 9, 10-13, 15, 23-26, 28 and 29)

ii. Contacting the sample with avian reovirus (claims 1, 7-10, 14, 15, 23-26, 28 and 29)

iii. Contacting the sample with adenovirus having a VA1 mutation (claims 23-26)

iv. Contacting the sample with vaccinia having a K3L mutation (claims 23-26)

v. Contacting the sample with vaccinia having a E3L mutation (claims 23-26)

vi. Contacting the sample with vaccinia having a K3L and a E3L mutation (claims 23-26)

vii. Contacting the sample with parapoxvirus orf viruses having a OV20.0L mutation (claims 23-26)

viii. Contacting the sample with influenza virus having a NS-1 mutation (claims 23-26)

ix. Contacting the sample with herpes virus having a gamma 34.5 mutation (claims 23-26)

x. Contacting the sample with vesicular stromatitis virus (claims 23-26)

xi. Contacting the sample with ONYX-015 virus (claims 23-26)

xii. Contacting the sample with Delta24 virus(claims 23-26)

Claim Objections

Claim 23 is objected to for being ungrammatical. Amending the claim to recite "indicates the presence of a neoplasm . . . " would overcome this objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8, 23-26, 28 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 1, 23, 25 and 28 are indefinite for omitting an essential step. Claims 1, 23, 25 and 28 are drawn to a method for detecting ras-activated neoplastic cells comprising contacting a sample with a reovirus, and determining the presence of a neoplasm if the reovirus is capable of replicating in the sample. However, there is no incubation step wherein the reovirus is contacted with the sample under conditions that support replication. The method requires an incubation step because the neoplasm diagnosis depends on the reovirus replicating in the sample. Claims 1, 23, 25 and 28 are therefore indefinite for omitting an essential step.

Claim 25 is indefinite in the recitation of "[a] method of detecting neoplastic cells having a particular phenotyope in a biological sample. . . ." It is unclear whether "having a particular phenotype in a biological sample" indicates (1) that the method detects neoplastic cells that behave a certain way (i.e. have a particular phenotype) in the biological sample, or (2) that the method detects whether neoplastic cells, having a certain phenotype, are present in the sample. The following language may be used to

convey the second interpretation: "[a] method for detecting neoplastic in a sample, wherein the neoplastic cells have a particular phenotype, the method comprising . . . ."

Claim 25 is also indefinite in the recitation of "a particular phenotype" since it is unclear what type of biological properties this language refers to. The specification also fails to provide an indication as to the meaning of the language "a particular phenotype." Claim 25 is therefore indefinite for failing to define the scope of the claimed invention.

Claim 28 is indefinite for the reasons discussed under claim 25 in that claim 28 recites "[a] method of diagnosing a neoplasm having a particular phenotype *in an animal* . . . ." Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section of the Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4-6, 25 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by "Strong" (Strong, J.E. "*The molecular basis of viral oncolysis: usurpation of the Ras signaling pathway by reovirus*" EMBO (1998) Vol. 17, No. 12, 3351-3362).

Claims 1, 2, 4-6 are interpreted as being drawn to a method for detecting ras-activated cells in a mammalian cell sample, wherein the method comprises contacting a mammalian cell sample with serotype 3 Dearing strain reovirus, and observing replication of the reovirus in the sample. Strong anticipates this method by disclosing the infection of a sample of ras-activated NIH-3T3 cells with serotype 3 Dearing strain reovirus, and observing the preferential killing of ras-transformed NIH-3TC cells in the sample (p. 3360, ¶ 1 and 8). Note that the limitation "wherein the ability of the reovirus to replicate indicates the presence of ras-activated neoplastic cells in the sample" does not distinguish the method from Strong. This results because this limitation merely recites a property that is inherent to cells that support reovirus replication. In other words, the claims lack a resolution step wherein the observation of reovirus replication is used to identify the presence of a neoplasm.

Claims 25 and 26 are drawn to a method of detecting cells with a particular phenotype, comprising contacting a biological sample with an oncolytic virus that replicates in cells having the particular phenotype, and observing the replication of the oncolytic virus. Strong anticipates this method by disclosing the killing of ras-activated mouse NIH-3T3 cells by infection with serotype 3 Dearing strain reovirus (p. 3360, ¶ 1 and 8). Note that the limitation "wherein the ability of the virus to replicate indicates the presence of neoplastic ells having the particular phenotype in the sample" does not distinguish claims 25 and 26 from Strong. As with claims 1, 2 and 4-6 above, this limitation merely states a property that is inherent to reovirus permissive cells.

Claims 1-6, 25 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by "Norman" (Norman, K.L. "*Reovirus as a novel oncolytic agent*" J. Clin. Invest. (April 2000) Vol. 105, No. 8, 1035-1038).

Claims 1-6, 25 and 26 are interpreted as being drawn to a method for detecting ras-activated cells in a human cell sample, wherein the method comprises the steps of contacting the human cell sample with

serotype 3 Dearing strain reovirus, and observing replication of the reovirus in the sample. Norman anticipates claims 1-6 in that it discloses infecting human ras-activated tumor cells with serotype 3 Dearing strain reovirus, and observing the replication of the reovirus in the human ras-activated tumor cells (see abstract, lines 8-12; and p. 1036, ¶ 4). Note that the limitation "wherein the ability of the reovirus to replicate indicates the presence of ras-activated neoplastic cells in the sample" does not distinguish the claimed method from Strong. As noted above, this limitation simply recites a property that is inherent to the infected cells. Based on the foregoing, Norman anticipates claims 1-6, 25 and 26.

Claims 1-6, 8, 25 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by "Coffey" (Coffey, M.C. "Reovirus Therapy of Tumors with Activated Ras Pathway" Science (November 1998) Vol. 282, 1332-1334).

Claims 1-6, 8, 25 and 26 are interpreted as noted above. Coffey discloses infecting a human central nervous system tumor cell (i.e. U87 gliolblastoma cells) with serotype 3 Dearing strain reovirus. Coffey therefore discloses the subject matter of claims 1-6, 25 and 26. Note that for the reasons stated above, claims 25 and 26 were not interpreted as requiring the step of identifying a ras-activated neoplasm.

Claims 1-6, 8, 25 and 26 are rejected under 35 U.S.C. 102(a) as being anticipated by "Hirasawa" (Hirasawa, K. "Oncolytic Reovirus against Ovarian and Colon Cancer" Cancer Res. (March 2002) Vol. 622, 1696-1701).

Claims 1-6, 8, 25 and 26 are interpreted as noted above. Hirasaw discloses infecting a human cancer cell lines with serotype 3 Dearing strain reovirus, and observing the preferential infection of tumor cells having a ras-activated phenotype (see e.g. abstract). Hirasawa therefore anticipates the subject matter of claims 1-6, 8, 25 and 26. Note that for the reasons stated above, claims 25 and 26 were not interpreted as requiring the step of identifying a ras-activated neoplasm.

Claims 23, 25, 26, 28 and 29 are rejected under 35 U.S.C. 102(e) as being anticipated by "Fueyo" (U.S. Pat. App. No. US2003/0138405 A1).

Claim 23 is interpreted as being drawn to a method of diagnosing a neoplasm in a mammal comprising contacting a sample of cells from the mammal with an oncolytic virus, and correlating the ability of the virus to replicate with the presence of a neoplasm in the sample. Fueyo, on the other hand, discloses a method for diagnosing a neoplasm in a human comprising the steps of obtaining a sample from the human (¶ 0238), exposing the sample to an oncolytic virus (¶ 0240), and determining the presence of a neoplasm based on the ability of the virus to replicate in the sample (Id.). Fueyo therefore anticipates the subject matter of claim 23.

Claims 25 and 26 are drawn to a method of detecting cells with a particular phenotype, comprising contacting a biological sample with an oncolytic virus that replicates in cells having the particular phenotype, and observing the replication of the oncolytic virus. Fueyo discloses a method for diagnosing a neoplasm having a specific phenotype comprising the steps of obtaining a sample from a human (¶ 0238), exposing the sample to oncolytic adenovirus (¶ 0240), and determining the presence of a defective Rb and/or p53 pathway based on the ability of the adenovirus to replicate in the sample (Id.). Fueyo therefore anticipates the subject matter of claims 25 and 26.

Claims 28 and 29 are interpreted as being drawn to a method of diagnosing a neoplasm having a particular cell phenotype in an animal comprising the steps of obtaining a sample of cells from the animal, contacting the sample with an oncolytic virus that requires the particular cell phenotype in order to replicate, observing replication of the virus in the sample of cells, and based on the replication, identifying the animal as having a neoplasm of the particular cell phenotype. Fueyo discloses a method for diagnosing a neoplasm having a specific phenotype comprising the steps of obtaining a sample from a

human (¶ 0238), exposing the sample to oncolytic adenovirus (¶ 0240), and determining the presence of a defective Rb and/or p53 pathway based on the ability of the adenovirus to replicate in the sample (Id.). Fueyo therefore anticipates the subject matter of claims 28 and 29.

Claim Rejections - 35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9-13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over "Fueyo" (U.S. Pat. App. No. US2003/0138405 A1) in view of "Norman" (Norman, K.L. "*Reovirus as a novel oncolytic agent*" J. Clin. Invest. (April 2000) Vol. 105, No. 8, 1035-1038).

Claims 9-13 and 15 are drawn to a method for diagnosing a ras-activated neoplasm in a human comprising the steps of providing a sample of cells from the human, contacting the sample of cells with serotype 3 Dearing strain reovirus, determining the ability of the reovirus to replicate in the sample, and identifying the animal as having a ras-activated neoplasm if the reovirus can replicate in the sample. The method further provides that the biological sample is from a neoplasm in the central nervous system.

Fueyo discloses a method for diagnosing an Rb- and/or p53-type neoplasm comprising the steps of providing a sample of human brain tissue (¶ 0238), exposing the sample to an oncolytic adenovirus (¶ 0240), and indicating the presence of an Rb- and/or p53-type neoplasm based on the ability of the adenovirus to replicate in the brain tissue sample (Id.). Fueyo does not expressly disclose a ras-activated neoplasm, or contacting the sample with reovirus. However, Norman teaches that reovirus replication is restricted to neoplasms with a ras-activated phenotype, and that normal cell phenotypes are resistant to reovirus. In light of Norman, one skilled in the art would appreciate that Fueyo's method could be practiced with reovirus in order to diagnose ras-activated neoplasms. Moreover, this combination would enjoy a reasonable expectation of success since both Fueyo and Norman rely on the same principles. That is, both methods diagnose a neoplasm based on the replication of a virus that is selective for a specific neoplastic phenotype.

Claims 8-13, 15 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over "Fueyo" (U.S. Pat. App. No. US2003/0138405 A1) in view of *"Strong" (Strong, J.E.* "The molecular basis of viral oncolysis: usurpation of the Ras signaling pathway by reovirus" *EMBO (1998) Vol. 17, No. 12, 3351-3362).*

Claims 8-13, 15 and 24 are drawn to a method for diagnosing a ras-activated neoplasm in a human comprising the steps of providing a sample of cells from the human, contacting the sample of cells with serotype 3 Dearing strain reovirus, determining the ability of the reovirus to replicate in the sample, and identifying the animal as having a ras-activated neoplasm if the reovirus can replicate in the sample. The method further provides that the biological sample may comprise a neoplasm from the central nervous system. Fueyo teaches all the limitations noted above. Fueyo does not expressly teach a ras-activated neoplasm, or contacting the sample with reovirus. However, Norman overcomes this deficiency by teaching that serotype 3 Dearing strain reovirus selectively replicates in cells having a ras-activated

phenotype (see e.g. abstract). This teaching would have motivated one skilled in the art to modify Fueyo's method to include exposing the sample to reovirus in order to identify neoplasms having a ras-activated phenotype. One skilled in the art would have a reasonable expectation of success applying reovirus to Fueyo's method because like the oncolytic adenovirus in Fueyo, Strong's reovirus only replicates in cells having a neoplastic phenotype. Therefore, at the time of Applicants' invention, it would have been obvious to modify Fueyo with Strong teachings in order to diagnose the presence of ras-activated neoplasms.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

i. Rubin et al. (U.S. Pat. No. 6,777,177 B1) 17 August 2004, Mammalian genes involved in viral infection and tumor suppression

ii. Sonenberg et al. (U.S. Pat. No. 5,670,330) 23 September 1997, Anti-tumor agent assay using PKR

iii. Norman et al. ''Reovirus Oncolysis of Human Breast Cancer'' Hum. Gene. Ther. (March 2002) Vol. 13, 641-652

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy M. Brown whose telephone number is (571) 272-0773. The examiner can normally be reached on Monday - Friday, 8am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached at (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Timothy M. Brown
Examiner
Art Unit 1648

tmb

James C. Housel 5/31/05

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